

In the claims:

Please amend the claims as follows:

**Claims 1-8. (Canceled)**

9. **(Previously presented)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a  $K_d$  of  $1 \times 10^{-10}$  M or less and a  $k_{off}$  rate constant of  $1 \times 10^{-3} s^{-1}$  or less, as determined by surface plasmon resonance.

10. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{off}$  rate constant of  $1 \times 10^{-4} s^{-1}$  or less.

11. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{off}$  rate constant of  $1 \times 10^{-5} s^{-1}$  or less.

12. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-9}$  M or less.

13. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-10}$  M or less.

14. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-11}$  M or less.

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**Claims 15-40. (Canceled)**

41. **(Original)** An isolated human antibody, or an antigen-binding portion thereof, which

a) inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-9}$ M or less;

b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and

c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

42. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27; and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

43. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29; and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

44. **(Original)** An isolated human antibody, or an antigen-binding portion thereof, having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 32.

45. **(Original)** The isolated human antibody of claim 44, comprising a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.

46. **(Original)** The isolated human antibody of claim 45, wherein the antibody heavy chain constant region is IgG1.

47. **(Original)** The isolated human antibody of claim 44, which is a Fab fragment.

48. **(Original)** The isolated human antibody of claim 44, which is a  $F(ab')_2$  fragment.

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49. **(Original)** The isolated human antibody of claim 44, which is a single chain Fv fragment.

Claims 50-87. **(Canceled)**

88. **(Previously presented)** A pharmaceutical composition comprising the antibody or an antigen binding portion thereof; of claim 9, 41, 44, 151, 153, 164, 167, 168, 172, 183, or 184, and a pharmaceutically acceptable carrier.

Claims 89-90 **(Canceled)**

91. **(Previously presented)** The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of budesonide, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, antibodies to IL-1 receptor, anti-IL-1 $\beta$  monoclonal antibodies, anti-IL-6 monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies.

Claims 92-141. **(Canceled)**

142. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 9, which is a recombinant antibody, or antigen-binding portion thereof.

143. **(Previously presented)** The isolated human antibody of any one of claims 9 to 11, wherein the antibody is a neutralizing antibody.

144. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* phytohemagglutinin blast proliferation assay (PHA assay) with an IC<sub>50</sub> of 1 x 10<sup>-7</sup> M or less.

145. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-8}$  M or less
146. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an  $IC_{50}$  of  $1 \times 10^{-10}$  M or less.
147. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an  $IC_{50}$  of  $1 \times 10^{-11}$  M or less.
148. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an  $IC_{50}$  of  $5 \times 10^{-12}$  M or less.
149. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-10}$  M or less.
150. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-11}$  M or less.
151. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $K_d$  of  $1 \times 10^{-10}$  M or less and binds to an epitope on the p40 subunit of human IL-12.
152. **(Previously presented)** The isolated human antibody of claim 151, which neutralizes the activity of human IL-12.
153. **(Currently amended)** A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a  $k_{off}$  rate constant of  $1 \times 10^{-2} s^{-1}$  to  $1 \times 10^{-3} s^{-1}$  or less, as determined by surface plasmon resonance.

154. **(Currently amended)** The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{\text{off}}$  rate constant of  $1 \times 10^{-4} \text{ s}^{-1}$  or less.

155. **(Previously presented)** The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{\text{off}}$  rate constant of  $1 \times 10^{-5} \text{ s}^{-1}$  or less.

156. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-7} \text{ M}$  or less

157. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-8} \text{ M}$  or less.

158. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-9} \text{ M}$  or less.

159. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-10} \text{ M}$  or less.

160. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $\text{IC}_{50}$  of  $1 \times 10^{-11} \text{ M}$  or less.

161. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $1 \times 10^{-10}$  M or less.

162. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $1 \times 10^{-11}$  M or less.

163. **(Currently amended)** The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $5 \times 10^{-12}$  M or less.

164. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, which

- a) dissociates from human IL-12 with a  $k_{\text{off}}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less, as determined by surface plasmon resonance;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

165. **(Previously presented)** The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{\text{off}}$  rate constant of  $1 \times 10^{-4} \text{ s}^{-1}$  or less.

166. **(Previously presented)** The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{\text{off}}$  rate constant of  $1 \times 10^{-5} \text{ s}^{-1}$  or less.

167. **(Previously presented)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and comprises:

- a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
- a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

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168. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

169. **(Previously presented)** The isolated human antibody, or an antigen-binding portion thereof, of claim 168, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 28 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 27.

170. **(Previously presented)** The isolated human antibody, or an antigen-binding portion thereof, of claim 169, wherein the LCVR further has CDR1 domain comprising the amino acid sequence of SEQ ID NO: 30 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 29.

171. **(Previously presented)** A pharmaceutical composition comprising an antibody or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody comprises:

a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and

a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

172. **(Previously presented)** An isolated human antibody that binds human IL-12 and is the antibody J695, or an antigen binding portion thereof.

173. **(Previously presented)** A pharmaceutical composition comprising the isolated human antibody of claim 172 and a pharmaceutically acceptable carrier.

Claims 174-182. **(Canceled)**

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183. **(Previously presented)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a  $K_d$  of  $1.34 \times 10^{-10}$  M or less, and neutralizes human IL-12.

184. **(Previously presented)** The isolated human antibody of claim 183, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $K_d$  of  $9.74 \times 10^{-11}$  M or less.

185. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claims 183 or 184, which is a recombinant antibody, or antigen-binding portion thereof.

186. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-7}$  M or less.

187. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-8}$  M or less.

188. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-9}$  M or less.

189. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-10}$  M or less.

190. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an  $IC_{50}$  of  $1 \times 10^{-11}$  M or less.

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191. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $1 \times 10^{-10}$  M or less.

192. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $1 \times 10^{-11}$  M or less.

193. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN $\gamma$  production with an IC<sub>50</sub> of  $5 \times 10^{-12}$  M or less.

194. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC<sub>50</sub> of  $1 \times 10^{-9}$  M or less.

195. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC<sub>50</sub> of  $1 \times 10^{-10}$  M or less.

196. **(Previously presented)** The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC<sub>50</sub> of  $1 \times 10^{-11}$  M or less.

197. **(Previously presented)** The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

198. **(Previously presented)** The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF $\beta$ , Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), p75TNFRlgG (Enbrel<sup>TM</sup>), p55TNFRlgG (Lenercept<sup>TM</sup>), pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP, mesalazine, chloroquine/hydroxychloroquine, pencillamine, aurothiomalate, cochlincine, salbutamol, terbutaline, salmeteral, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium, and oxitropium.

199. **(Previously presented)** The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, D2E7, cA2 (Remicade<sup>TM</sup>), CDP 571, 5-aminosalicylic acid, TNFR-Ig constructs, dexamethasone, aminosalicylic acid, IL-1ra, methylprednisolone, cyclophosphamide, methotrexate, 4-aminopyridine, tizanidine, interferon- $\beta$ 1a (Avonex<sup>TM</sup>), interferon- $\beta$ 1b (Betaseron<sup>TM</sup>), Copolymer 1 (Cop-1; Copaxone<sup>TM</sup>), hyperbaric oxygen, clabribine, anti-EMAP-II antibodies, IFN $\beta$ 1a, IFN $\beta$ 1b, and IL-1.

200. **((Previously presented))** A pharmaceutical composition comprising the antibody or an antigen binding portion thereof of claim 143, and a pharmaceutically acceptable carrier.

201. **(Previously presented)** The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of budenoside, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, antibodies to IL-1 receptor, anti-IL-1 $\beta$  monoclonal antibodies, anti-IL-6

monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies.

**202. (Previously presented)** The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

**203. (Previously presented)** The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF $\beta$ , Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), p75TNFRlgG (Enbrel<sup>TM</sup>), p55TNFRlgG (Lenercept<sup>TM</sup>), pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP, mesalazine, chloroquine/hydroxychloroquine, pencillamine, aurothiomalate, cochlaine, salbutamol, terbutaline, salmeterol, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium, and oxitropium.

**204. (Previously presented)** The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, D2E7, cA2 (Remicade<sup>TM</sup>), CDP 571, 5-aminosalicylic acid, TNFR-Ig constructs, dexamethasone, aminosalicylic acid, IL-1ra, methylprednisolone, cyclophosphamide, methotrexate, 4-aminopyridine, tizanidine, interferon- $\beta$ 1a (Avonex<sup>TM</sup>), interferon- $\beta$ 1b

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(Betaseron<sup>TM</sup>), Copolymer 1 (Cop-1; Copaxone<sup>TM</sup>), hyperbaric oxygen, clabribine, anti-EMAP-II antibodies, IFN $\beta$ 1a, IFN $\beta$ 1b, and IL-1.

205. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a  $K_d$  of  $1.34 \times 10^{-10}$  M or less.

206. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a  $K_d$  of  $9.74 \times 10^{-11}$  M or less.

207. **(New)** The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a  $k_{off}$  rate constant of  $1 \times 10^{-3} \text{ s}^{-1}$  or less.